## (FILE 'HOME' ENTERED AT 17:44:38 ON 18 JAN 2011)

FILE 'MEDLINE, CAPLUS, BIOSIS, SCISEARCH, LIFESCI' ENTERED AT 17:45:14 ON 18 JAN 2011

- L1 337539 S OSTEOBLAST OR MYOBLAST OR CHONDROCYTE OR ADIPOCYTE
- L2 21589 S DEDIFFERENTIAT?
- L3 53262 S MESENCHYMAL (3A) STEM (W) CELL
- L4 2363 S L1(P)L2
- L5 103 S L4(P)L3
- L6 45 DUP REM L5 (58 DUPLICATES REMOVED)
- => d au ti so pi 20-45 16
- L6 ANSWER 20 OF 45 MEDLINE on STN
- AU Boeuf S; Steck E; Pelttari K; Hennig T; Buneb A; Benz K; Witte D; Sultmann H; Poustka A; Richter W
- TI Subtractive gene expression profiling of articular cartilage and mesenchymal stem cells: serpins as cartilage-relevant differentiation markers.
- SO Osteoarthritis and cartilage / OARS, Osteoarthritis Research Society, (2008 Jan) Vol. 16, No. 1, pp. 48-60. Electronic Publication: 2007-07-02. Journal code: 9305697. ISSN: 1063-4584. L-ISSN: 1063-4584.
- L6 ANSWER 21 OF 45 MEDLINE on STN DUPLICATE 10
- AU Khan I M; Gilbert S J; Singhrao S K; Duance V C; Archer C W
- TI Cartilage integration: evaluation of the reasons for failure of integration during cartilage repair. A review.
- SO European cells & materials, (2008) Vol. 16, pp. 26-39. Electronic Publication: 2008-09-03. Ref: 108
  Journal code: 100973416. E-ISSN: 1473-2262. L-ISSN: 1473-2262.
- L6 ANSWER 22 OF 45 CAPLUS COPYRIGHT 2011 ACS on STN
- IN Son, Young Sook; Lee, Jung Sun; Lee, Eun Kyung; Lee, Jin Yeon
- TI Artificial cartilage containing chondrocytes obtained from costal cartilage and preparation process thereof
- SO PCT Int. Appl., 76 pp.

CODEN: PIXXD2

|    | PATENT NO.    |               |     |     |     | KIN         | )    | DATE     |                | APPLICATION NO.  |     |     |          |     | DATE     |     |     |     |
|----|---------------|---------------|-----|-----|-----|-------------|------|----------|----------------|------------------|-----|-----|----------|-----|----------|-----|-----|-----|
| ΡI | WO 2007052935 |               |     |     |     | A1          |      | 20070510 |                | WO 2006-KR4479   |     |     |          |     | 20061031 |     |     |     |
|    |               | W:            | ΑE, | AG, | AL, | ΑM,         | ΑT,  | ΑU,      | AZ,            | BA,              | BB, | BG, | BR,      | BW, | BY,      | BZ, | CA, | CH, |
|    |               |               | CN, | CO, | CR, | CU,         | CZ,  | DE,      | DK,            | DM,              | DZ, | EC, | EE,      | EG, | ES,      | FΙ, | GB, | GD, |
|    |               |               | GE, | GH, | GM, | GT,         | HN,  | HR,      | HU,            | ID,              | IL, | IN, | IS,      | JP, | ΚE,      | KG, | KM, | KN, |
|    |               |               | KP, | KΖ, | LA, | LC,         | LK,  | LR,      | LS,            | LT,              | LU, | LV, | LY,      | MA, | MD,      | MG, | MK, | MN, |
|    |               |               | MW, | MX, | MY, | MZ,         | NA,  | NG,      | NΙ,            | NO,              | NΖ, | OM, | PG,      | PH, | PL,      | PT, | RO, | RS, |
|    |               |               | RU, | SC, | SD, | SE,         | SG,  | SK,      | SL,            | SM,              | SV, | SY, | ΤJ,      | TM, | TN,      | TR, | TT, | TZ, |
|    |               |               | UA, | UG, | US, | UZ,         | VC,  | VN,      | ZA,            | ZM,              | ZW  |     |          |     |          |     |     |     |
|    |               | RW:           | AT, | BE, | BG, | CH,         | CY,  | CZ,      | DE,            | DK,              | EE, | ES, | FI,      | FR, | GB,      | GR, | HU, | ΙE, |
|    |               |               | IS, | ΙT, | LT, | LU,         | LV,  | MC,      | NL,            | PL,              | PT, | RO, | SE,      | SI, | SK,      | TR, | BF, | ВJ, |
|    |               |               | CF, | CG, | CI, | CM,         | GA,  | GN,      | GQ,            | GW,              | ML, | MR, | NE,      | SN, | TD,      | ΤG, | BW, | GH, |
|    |               |               | GM, | ΚE, | LS, | MW,         | MZ,  | NA,      | SD,            | SL,              | SZ, | TZ, | UG,      | ZM, | ZW,      | ΑM, | ΑZ, | BY, |
|    |               |               | KG, | KΖ, | MD, | RU,         | ΤJ,  | TM       |                |                  |     |     |          |     |          |     |     |     |
|    | KR            | 2007046768    |     |     | Α   |             | 2007 | 0503     | KR 2006-106812 |                  |     |     | 20061031 |     |          |     |     |     |
|    | KR            | 917422        |     |     | В1  | 31 20090922 |      |          |                |                  |     |     |          |     |          |     |     |     |
|    | EP 1954802    |               |     |     |     | A1          |      | 2008     | 0813           | EP 2006-812318   |     |     |          |     | 20061031 |     |     |     |
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|    |               |               | IS, | ΙT, | LI, | LT,         | LU,  | LV,      | MC,            | NL,              | PL, | PT, | RO,      | SE, | SI,      | SK, | TR  |     |
|    | US            | S 20090228105 |     |     | A1  | A1 20090910 |      |          | US 2008-159204 |                  |     |     |          |     | 20080625 |     |     |     |
|    | CN            | N 101589139   |     |     | А   | 20091125    |      |          |                | CN 2006-80049510 |     |     |          |     | 20080627 |     |     |     |

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- AU Guldberg, Robert E. (Reprint); Coleman, Rhima M.; Case, Natasha D.
- TI Hydrogel effects on bone marrow stromal cell response to chondrogenic growth factors
- SO BIOMATERIALS, (APR 2007) Vol. 28, No. 12, pp. 2077-2086. ISSN: 0142-9612.
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- AU Lysy Philippe A; Smets Francoise; Sibille Catherine; Najimi Mustapha; Sokal Etienne M
- TI Human skin fibroblasts: From mesodermal to hepatocyte-like differentiation.
- SO Hepatology (Baltimore, Md.), (2007 Nov) Vol. 46, No. 5, pp. 1574-85. Journal code: 8302946. E-ISSN: 1527-3350. L-ISSN: 0270-9139.
- L6 ANSWER 25 OF 45 CAPLUS COPYRIGHT 2011 ACS on STN
- AU Diaz-Romero, Jose; Nesic, Dobrila; Grogan, Shawn Patrick; Heini, Paul; Mainil-Varlet, Pierre
- TI Immunophenotypic changes of human articular chondrocytes during monolayer culture reflect bona fide dedifferentiation rather than amplification of progenitor cells
- SO Journal of Cellular Physiology (2007), Volume Date 2008, 214(1), 75-83 CODEN: JCLLAX; ISSN: 0021-9541
- L6 ANSWER 26 OF 45 CAPLUS COPYRIGHT 2011 ACS on STN
- AU Chen, Guoping; Kawazoe, Naoki; Tateishi, Tetsuya; Tanaka, Junzo
- TI Control of cell functions by hybrid biodegradable polymer scaffolds
- SO Materials Integration (2007), 20(11), 8-13 CODEN: MINTFB; ISSN: 1344-7858
- L6 ANSWER 27 OF 45 SCISEARCH COPYRIGHT (c) 2011 The Thomson Corporation on STN
- AU Zheng M H (Reprint); Lin Z; Willers C; Xu J A
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- L6 ANSWER 28 OF 45 SCISEARCH COPYRIGHT (c) 2011 The Thomson Corporation on STN
- AU Nagashima H (Reprint); Shimada A; Tomii R; Kano K
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- SO BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, (2 JUN 2006) Vol. 344, No. 2, pp. 455-462. ISSN: 0006-291X.
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- AU Sakuma, Takahiro; Matsumoto, Taro; Kano, Koichirou; Takahashi, Satoru; Muishima, Hideo
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- AU Goessler Ulrich Reinhart; Bieback Karen; Bugert Peter; Heller Tobias; Sadick Haneen; Hormann Karl; Riedel Frank
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- TI Induction of intervertebral disc-like cells from adult mesenchymal stem cells.
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- TI Immunophenotypic analysis of human articular chondrocytes: changes in surface markers associated with cell expansion in monolayer culture
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- TI Characterization and chondrocyte differentiation stage-specific expression of KRAB zinc-finger protein gene ZNF470
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- AU Imabayashi Hideaki; Mori Taisuke; Gojo Satoshi; Kiyono Tohru; Sugiyama Tomoyasu; Irie Ryotaro; Isogai Takao; Hata Jun-ichi; Toyama Yoshiaki; Umezawa Akihiro
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- SO Experimental cell research, (2003 Aug 1) Vol. 288, No. 1, pp. 35-50. Journal code: 0373226. ISSN: 0014-4827. L-ISSN: 0014-4827.
- L6 ANSWER 43 OF 45 MEDLINE on STN DUPLICATE 22
- AU Tagami Motoki; Ichinose Shizuko; Yamagata Kazuo; Fujino Hideaki; Shoji Satoshi; Hiraoka Masayasu; Kawano Seiko
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- => d ab 41-45 16
- L6 ANSWER 41 OF 45 MEDLINE on STN DUPLICATE 20
- PURPOSE OF REVIEW: This review addresses the progress in three major AB fields of "genomics of osteoarthritis" over the past year: genetic alterations thought to be important for the initiation and progression of osteoarthritis, differential gene expression analysis, and functional genomics of osteoarthritis. RECENT FINDINGS: Distinct genetic risk factors may predispose different joint sites to osteoarthritis, and although clear loci for susceptibility genes for common osteoarthritis have yet to emerge from the epidemiological studies, new approaches are narrowing down known loci. The search for specific genes using cDNA array technology has further demonstrated its potential in arthritis research as a powerful tool that could further provide biological insights into disease mechanisms, osteoarthritis polymorphic subtypes, the molecular validation of animal models, and the monitoring of drug activity on gene expression levels. Gene expression analysis has further characterized the striking shift in the gene expression pattern during " dedifferentiation" of chondrocytes in vitro as well as added depth to the phenotype of differentiated versus undifferentiated mesenchymal stem cells. Several new molecules potentially relevant to the disease process were identified, among them beta2-microglobulin (B2M), clusterin, and chitinase-like molecule 2. SUMMARY: Functional genomic approaches will in the future allow to complement traditional biochemistry and molecular biology. Although there are limitations to cDNA array technology, "molecular portraits" of osteoarthritic chondrocytes in vivo and in vitro can be produced to analyze whole or large biologic systems rather than just single aspects of it. This will stimulate the testing of new markers, which are needed for the diagnosis and monitoring of osteoarthritis.
- ANSWER 42 OF 45 MEDLINE on STN DUPLICATE 21 L6 Characterization of dedifferentiated chondrocytes AΒ (DECs) and mesenchymal stem cells capable of differentiating into chondrocytes is of biological and clinical interest. We isolated DECs and bone marrow stromal cells (BMSCs), H4-1and H3-4, and demonstrated that the cells started to produce extracellular matrices, such as type II collagen and aggrecan, at an early stage of chondrosphere formation. Furthermore, cDNA sequencing of cDNA libraries constricted by the oligocapping method was performed to analyze difference in mRNA expression profiling between DECs and marrow stromal cells. Upon redifferentiation of DECs, cartilage-related extracellular matrix genes, such as those encoding leucine-rich small proteoglycans, cartilage oligomeric matrix protein, and chitinase 3-like 1 (cartilage glycoprotein-39), were highly expressed. Growth factors such as FGF7 and CTGF were detected at a high frequency in the growth stage of monolayer stromal cultures. By combining the expression profile and flow cytometry,

we demonstrated that isolated stromal cells, defined by CD34(-), c-kit(-), and CD140alpha(- or low), have chondrogenic potential. The newly established human mesenchymal cells with expression profiling provide a powerful model for a study of chondrogenic differentiation and further understanding of cartilage regeneration in the means of redifferentiated DECs and BMSCs.

L6 ANSWER 43 OF 45 MEDLINE on STN

DUPLICATE 22

We examined human bone marrow mesenchymal stem AΒ cells by applying real-time quantitative polymerase chain reaction (PCR) (RT-PCR) technology and electron-microscopic techniques. Our RT-PCR demonstrated that the values of peroxisome proliferation-activated receptor gamma2 (PPARgamma2) and lipoprotein lipase (LPL) mRNA dramatically increased according to adipogenic stimulation. The expressions of both PPARgamma2 and LPL mRNA were significantly reduced ( P<0.01) and almost disappeared after stimulation had ceased. The expressions of both genes, however, increased again by stimulation even though the cells were in a dedifferentiated state for a month. In the ultrastructural study, over 80% of the cells proceeded into morphologically well-developed adipocytes at the 12th day of induction/maintenance which were packed with lipid droplets and clusters. In the next process these lipid products were excreted from the cell bodies and the peripheral small parts containing numerous droplets were torn from the greater parts, which stuck tightly to each other and adhered to culture dishes. Adipocytes were not detected in the culture media during the final stage. The total cell number was equal to and over 90% of the cells dedifferentiated into fibroblast-like stem cells during the final maintenance period of 1 month. Furthermore the dedifferentiated cells quickly differentiated again into adipocytes by stimulation even if they were quiescent for 1 month. Thus we conclude that mesenchymal stem cells have strong reversibility from both the genetic and morphological points of view.

L6 ANSWER 44 OF 45 MEDLINE on STN DUPLICATE 23

AΒ Biopsies removed from 57 patients considered for cartilage transplantation were grown at CTI Ltd. (47 biopsies) and at Tel Aviv University (10 biopsies). Tissue processing took place in dedicated laboratories. Explant cultures allowed cell number expansion. Fifty-four out of 57 biopsies grew cells. Fanning out of the cells began after 5-15 days in culture. Two passages later, cell numbers in the 10(7) range were achieved. Cells from all cultures expressed mRNA of aggrecan and link protein but not of alkaline phosphatase. Histochemical stains such as alcian blue pH 1 were negative in sparse monolayer cultures, but positive in pellet cultures. Immunohistochemistry demonstrated expression of collagen type I in monolayer cultures, switching to collagen type II in micromass cultures. Fibroblast growth factor receptor 3, a recently described characteristic receptor of precartilaginous cells, was expressed in monolayers and disappeared in micromass cultures. In conclusion, explants of articular chondrocytes cultured in vitro consistently yield monolayer cultures. The cells appear to revert to dedifferentiated chondrocytes, expressing a mesenchymal stem cell protein profile. Simultaneously, these cells regained their capacity to proliferate. Cultures held as micromass allowed reexpression of the differentiated phenotype traits.

L6 ANSWER 45 OF 45 MEDLINE on STN DUPLICATE 24

AB The expression of defects in the control of cellular differentiation is thought to be of etiological significance in the early stages of carcinogenesis. This possibility is supported by a variety of

experimental studies including those that have established that metaplastic changes in cells can represent preneoplastic lesions in vivo. To evaluate this question in greater detail, we have used 3T3 T mesenchymal stem cells as a model system. These cells express certain characteristics of preneoplastic cells even though they can regulate their proliferation and even though they can undergo nonterminal and terminal differentiation into adipocytes . For example, they are immortal and aneuploid, and they show a proclivity to undergo spontaneous or induced neoplastic transformation compared to normal human cells. The question we sought to answer in the current experiments concerns whether predifferentiation growth arrest and/or nonterminal differentiation in such preneoplastic cells is completely reversible or whether these processes induce the expression of the new stable program that limits the cells' proliferative potential and reduces the cells' subsequent differentiation potential in a manner comparable to that which is thought to occur in normal stem cells. The results show that arrest at both the predifferentiation state and at the nonterminal differentiation state is a completely reversible phenomenon that does not limit the cells' subsequent growth or differentiation potential. In fact, the results show that, when nonterminally differentiated 3T3 T adipocytes are induced to dedifferentiate, they can subsequently redifferentiate into macrophages. We therefore suggest that preneoplasia as expressed in 3T3 T mesenchymal stem cells is associated with the expression of defects in the ability to integrally control cellular differentiation and proliferation. As a result, the data suggest that such cells express an increased proclivity to undergo metaplastic change and complete neoplastic transformation.